

PATENT
512585-2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Tagg *et al.*
Serial No. : 09/913,763
Filed : August 17, 2001
For : LANTIBIOTIC
Art Unit : 1651
Examiner : Michael V. Meller

745 Fifth Avenue, New York, NY 10151

EXPEDITED PROCEDURE
RESPONSE AFTER FINAL ACTION
UNDER 37 C.F.R. 1.116

DRAFT
FOR DISCUSSION PURPOSES ONLY

AMENDMENT AFTER FINAL ACTION UNDER 37 C.F.R. §1.116

Commissioner for Patents
Washington, D.C. 20231
Box AF

Dear Sir:

This is in response to the final Office Action mailed on June 3, 2003, setting a three-month term for reply.

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AMENDMENT

Please amend the application without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents.

In the Claims

1. (Currently amended) An isolated bacteriocidal ~~antibacterial~~ protein obtainable ~~obtained~~ from *Streptococcus salivarius* strain K12 on deposit at Deutsche Sammlung von Mikroorganismen Und Zellkulturen GmbH, Braunschweig, Germany, accession number DSM 13084, having the following properties:

a) — a molecular mass of approximately 2733 Da, as determined by ion-spray mass spectrometry, and an N-terminal amino acid sequence represented by SEQ ID NO: 1, ~~or~~

b) — ~~an antibacterial variant of the antibacterial protein, which variant has greater than 80% amino acid sequence identity with said protein.~~ ^{new issue}

2. (Cancelled)

3. (Allowed) An isolated antibacterial protein having the amino acid sequence of SEQ ID NO: 3. ^{allowable.}

4. (Currently amended) An isolated bacteriocidal ~~antibacterial~~ protein which has an amino acid sequence which differs from the sequence of SEQ ID NO: 3 by the insertion, deletion or substitution of from one to three amino acids, ^{wherein}

5. (Cancelled)

6. (Currently amended) [[A]]The protein as claimed in any one of claims 1, 3 or 4, ~~claim 5~~ which is bacteriocidal with respect to *Streptococcus pyogenes*.

7. (Currently amended) An antibacterial composition which includes [[a]]the protein as claimed in any one of claims 1, 3, 4 or 6 [[to 6]] or an organism which can express [[a]]the protein as claimed in any one of claims 1, 3, 4 or 6 [[to 6]].

8. (Currently amended) A therapeutic formulation which comprises:

(i) [[a]]the protein as claimed in any one of claims 1, 3, 4 or 6 [[-6]]; or

(ii) ~~an organism which can express~~ ^{*Streptococcus salivarius*} the [[a]] protein as claimed in any one of claims 1, 3, 4 or 6 [[-6]],

in combination with a diluent, carrier and/or excipient.

9. (Cancelled)

10. (Cancelled)

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11. (Currently amended) ~~[[A]]~~The therapeutic formulation as claimed in claim 8, any one of claims 8-10 which is an orally administrable medicament.
12. (Currently amended) ~~A medicament~~ The therapeutic formulation as claimed in claim 11, wherein the medicament ~~which~~ is a syrup, mouthwash, gargle, toothpaste or mouth spray.
13. (Currently amended) ~~A medicament~~ The therapeutic formulation as claimed in claim 11, wherein the medicament ~~which~~ is in a unit dosage form.
14. (Currently amended) ~~A medicament~~ The therapeutic formulation as claimed in claim 12, wherein the medicament ~~which~~ is a lozenge or capsule ~~containing a unit dose of an organism which can express a protein as claimed in any one of claims 1-6.~~
15. (Currently amended) ~~[[A]]~~The therapeutic formulation as claimed in claim 8 any one of claims 8-11 in which said protein or organism is included in a food or drink.
16. (Currently amended) ~~[[A]]~~The therapeutic formulation as claimed in claim 15 in which said food or drink is a dairy product based food or drink.
17. (Currently amended) ~~[[A]]~~The therapeutic formulation as claimed in claim 16 in which said protein or organism is included in milk powder, milk biscuits, milk, yoghurt or cheese.
18. (Currently amended) ~~[[A]]~~The therapeutic formulation as claimed in claim 16 in which said protein or organism is included in a flavoured milk.
19. (Currently amended) ~~[[A]]~~The therapeutic formulation as claimed in claim 8, any one of claims 8-10 in which said protein or organism is included in a confectionery.
20. (Currently amended) ~~[[A]]~~The therapeutic formulation as claimed in claim 19 in which said confectionery is a chewing gum.
21. (Currently amended) ~~[[A]]~~The therapeutic formulation as claimed in claim 8, any one of claims 9-20 which further comprises one or more secondary antibacterial agents.
22. (Currently amended) ~~[[A]]~~The therapeutic formulation as claimed in claim 21 in which said secondary antibacterial agent(s) are selected from bacteriocin-like inhibitory substance(s) (BLIS).
23. (Currently amended) ~~[[A]]~~The therapeutic formulation as claimed in claim 20 which includes one or more ~~both~~ of Salivaricin A, an organism which ~~can~~ expresses Salivaricin A, the an antibacterial protein which has the amino acid sequence of SEQ ID NO:5, or an

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organism which can express the antibacterial protein which has the amino acid sequence of SEQ ID NO:5.

24. (Withdrawn) A polynucleotide which encodes a protein as claimed in any one of claims 1-6.

25. (Withdrawn) A polynucleotide which comprises the coding sequence of SEQ ID NO: 2.

26. (Withdrawn) A polynucleotide as claimed in claim 24 which comprises a DNA sequence which encodes an antibacterial protein as claimed in claim 1 which is part of the genome of *S. salivarius* strain K12, on deposit at Deutsche Sammlung von Mikroorganismen Und Zellkulturen GmbH, Braunschweig, Germany, accession number DSM 13084.

27. (Currently amended) ~~An organism~~ *Streptomyces salivarius* strain K12 DSM 13084, in substantially pure form, which includes a polynucleotide which:

a) encodes a protein as claimed in any one of claims 1, 3, 4 or 6[[-6]]; or

b) comprises the coding sequence of SEQ ID NO:2; or

~~c) encodes a protein as claimed in any one of claims 1-6, comprising the DNA sequence which encodes an antibacterial protein as claimed in claim 1, which is part of the genome of *S. salivarius* strain K12, on deposit at Deutsche Sammlung von Mikroorganismen Und Zellkulturen GmbH, Braunschweig, Germany, accession number DSM 13084.~~

28. (Currently amended) ~~[[An]]~~ The organism as claimed in claim 27 in which said polynucleotide is heterologous to the organism.

29. (Currently amended) ~~[[An]]~~ The organism as claimed in claim 27 which is a *S. salivarius* organism.

30. (Original) A biologically pure culture of *S. salivarius* strain K12, on deposit at Deutsche Sammlung von Mikroorganismen Und Zellkulturen GmbH, Braunschweig, Germany, accession number DSM 13084.

31. (Original) A biologically pure culture of *S. salivarius* strain K30 on deposit at Deutsche Sammlung von Mikroorganismen Und Zellkulturen GmbH, Braunschweig, Germany, accession number DSM 13085.

32. (Original) A therapeutic formulation which includes *S. salivarius* strain K12 or *S. salivarius* strain K30 as identified in claim 30 or claim 31.

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33. (Currently amended) A method of treating an individual to at least inhibit growth of harmful streptococcal bacteria in the upper respiratory tract, comprising the step of administering an effective amount of ~~[[a]]~~the protein as claimed in any one of claims 1, 3, 4 or 6~~[[6]]~~ orally to said individual.

34. (Currently amended) A method of treating an individual to at least inhibit growth of harmful streptococcal bacteria in the upper respiratory tract, comprising the step of administering as claimed in claim 33 in which said protein is administered orally to said individual as part of a therapeutic formulation as claimed in any one of claims 8 to 23 and 32 claim 8 orally to said individual.

35. (Currently amended) ~~[[A]]~~The method as claimed in claim 33 wherein said inhibitory effect is caused by colonising at least part of the upper respiratory tract of an individual with a viable organism in substantially pure form which expresses said protein.

36. (Currently amended) ~~[[A]]~~The method as claimed in claim 35 wherein said organism is administered as part of a medicament, a food or drink or a confectionery.

37. (Currently amended) ~~[[A]]~~The method as claimed in claim 35 ~~or claim 36~~ wherein said organism is a *S. salivarius* strain selected from strains K12 and K30.

38. (Currently amended) ~~[[A]]~~The method as claimed in claim 33 ~~any one of claims 33-37~~ which includes a preliminary step of pre-treating said individual to at least reduce the bacterial population present in the upper respiratory tract.

39. (Currently amended) ~~[[A]]~~The method as claimed in claim 38 wherein said pre-treatment comprises the step of administering an antibiotic orally to said individual.

40. (Currently amended) A method of treatment of a patient against infections of the upper respiratory tract caused by streptococcal organisms which comprises the steps of:

- (i) orally administering to said patient an amount of an antibiotic effective to reduce the numbers of streptococci present, thereby generating a bacterially depopulated environment; and
- (ii) administering, to the ~~resulting~~ bacterially depopulated environment, *S. salivarius* organism(s) in substantially pure form which produce BLIS to repopulate said environment.

41. (Withdrawn) An antibacterial ~~protein~~ which has the amino acid sequence of SEQ ID NO: 5.

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42. (Withdrawn) A polynucleotide which includes the coding sequence of SEQ ID NO: 4.
43. (Withdrawn) A therapeutic formulation which comprises an antibacterial protein as claimed in claim 41, in combination with a diluent, carrier and/or excipient.
44. (Withdrawn) A therapeutic formulation which contains an antibacterial protein as claimed in any one of claims 1-6 and an antibacterial protein as claimed in claim 41.
45. (Withdrawn) A therapeutic formulation which contains at least one *S. salivarius* organism which expresses an antibacterial protein as claimed in any one of claims 1-6 and at least one other *S. salivarius* organism which expresses an antibacterial protein as claimed in claim 41.
46. (Withdrawn) An isolated polypeptide encoded by the amino acid sequence of SEQ ID NO: 3, or a fragment or variant thereof, wherein the variant has greater than 80% amino acid sequence homology to SEQ ID NO: 3, and wherein the polypeptide is bacteriocidal.